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Indicators for peracid vapour sterilisation - comprising filter paper
impregnated with rapidly bleachable dye

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Test papers for monitoring sterilisation by percarboxylic (esp.
peracetic) acid vapours comprise filter paper that has been impregnated
with a dye soln. and dried. The dye can undergo rapid oxidative
bleaching.

USE/ADVANTAGE - The test papers may be used to monitor
sterilisation of heat sensitive instruments in autoclaves, esp. in
medical and pharmaceutical fields. The papers provide a simple and
rapid test to assess the effectiveness of sterilisation procedures.

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A Commerce Patent (WP)

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Title: A Control Indicator for the Gas-Sterilization

Keywords:

Control indicator, gas-sterilization, autoclave, percarboxylic acid vapors, peracetic acid vapors, crystal violet, oxidative decolorization.

Abstract:

A control indicator is described for the gas-sterilization of objects and instruments with percarboxylic acid vapors, preferably peracetic acid vapors, in a closed chamber or in an autoclave, respectively. The application occurs in particular in health-care facilities, as well as also in the pharmaceutical industry. The control indicator will permit the determination, whether or not the packaged materials to be sterilized have already been subjected to the sterilization process, whereby a mix-up with a not yet treated material will be prevented. A filter-paper strip impregnated e.g. with a crystal violet solution, is well suited as a control indicator, whereby this colored filter paper will be quickly decolorized (bleached) by the per-acid vapors.

PATENT CLAIMS

1. A control indicator for the gas-sterilization for testing the performed sterilization process with percarboxylic acid vapors, preferably peracetic acid vapors, consisting e.g. of a filter paper impregnated with certain dye solutions of a defined concentration and subsequently dried, wherein the dye solutions contain one or several oxidatively fast bleachable dyes.
2. A control indicator according to claim 1, wherein the oxidatively fast bleachable dyes preferably consist of crystal violet, Victoria blue, China blue, cotton blue, gentiana violet, methyl violet, light green, malachite green, diamond fuchsin, fuchsin basic or fuchsin acidic.
3. A sterilization indicator according to claim 1 and 2, wherein the dye solutions advantageously consist of a 0.5% solution of crystal violet in water.

Application Field of the Invention

The invention deals with a control indicator for the testing of the already performed gas-sterilization of objects and instruments, in particular heat-sensitive instruments, in a closed chamber, preferably an autoclave, respectively. The application occurs in particular in health-care facilities, as well as in the pharmaceutical industry.

Characteristics of the known State of the Art

In addition to the already known processes, which have been in practical use for a long time, such as the gas-sterilization process with ethylene oxide and formaldehyde, the gas-sterilization with percarboxylic acid vapors has been introduced. Furthermore, the biological control of the gas-sterilizers with specially prepared strips of *bacillus subtilis* or *bacillus stearothermophilus*, has been well known, whereby this control is to be performed in defined time intervals, e.g. semi-annually, by placing a larger number of these test-strips at the various locations within the sterilization chamber. For determining the functioning of the sterilizer, the bio-indicators have to be incubated for several days. However, no conclusions may be drawn, whether or not the packaged objects to be sterilized, have already been treated in the sterilization process. These types of control indicators, also often called treatment indicators, for the gas-sterilization with percarboxylic acid vapors have not been known.

Objectives of the Invention

The objectives to be achieved by the invention deal with the development of an indicator for the daily sterilization with peracetic acid vapors in a closed chamber or an autoclave, respectively, whereby the occurred sterilization process will be indicated and a mix-up with still untreated objects and materials will be prevented.

Presentation of the Essence of the Invention

The objectives of the invention deal with the development of an indicator for indicating the performed sterilization of the packaged objects and materials to be sterilized with e.g. peracetic acid vapors, whereby the already occurred sterilization will be indicated by optically readily recognizable changes in the appearance for preventing a mix-up with still untreated items or materials and, thereby, for assuring a fast control of the treatment procedure. Since the rate of the decolorization process is different depending on the stability of the particular dye against an oxidation, a dye had to be found, which is suited for a high-quality control indicator.

The objectives have been achieved according to the invention by utilizing the strong oxidizing and bleaching effects of the peracetic acid vapors on dyes suited for this purpose.

According to the invention, a 0.5% solution of crystal violet in water is used. However, the following aqueous dye solutions may e.g. also be employed: Victoria blue, China blue, cotton blue, gentiana violet, methyl violet, light green, malachite green, diamond fuchsin, fuchsin basic and fuchsin acidic. The indicator is to be attached onto the packaged items to be kept sterile and/or placed into the packages.

Execution Example

The filter paper to be used for the preparation of the indicator, will be immersed into the respective dye solution for about 5 minutes and subsequently be dried e.g. by a suspension in air. According to *P.G. Simon, Hygiene and Medicine* 12, 416 (1987), chemical indicators are to have a minimal surface area of 1 cm², but not more than maximal 3.5 cm². These indicators are attached onto the packages to be sterilized and/or placed into the packages.

The prepared control indicators exhibit a very good storability, if not directly exposed to sunlight for a longer period of time.

At 45°C and an initial vacuum of 2.66 KPa (= 20 mm Hg) in a glass desiccator, the filter paper impregnated with a 0.5% crystal violet solution, will be completely decolorized by peracetic acid vapors within 5 to 10 minutes.

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(54) Kontrollindikator für die Gassterilisation

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(57) Kontrollindikator für die Gassterilisation von Gegenständen und Instrumenten mit Perkarbonsäuredämpfen, vorzugsweise Peressigsäuredämpfen, in einer geschlossenen Kammer bzw. in einem Autoklav. Die Anwendung erfolgt insbesondere in den Einrichtungen des Gesundheitswesens sowie in der pharmazeutischen Industrie. Der Kontrollindikator ermöglicht es festzustellen, ob das zu sterilisierende verpackte Material den Sterilisationsprozeß durchlaufen hat, damit Verwechslungen mit noch nicht behandeltem Material ausgeschlossen werden können. Geeignet ist z. B. mit Kristallviolett angefärbtes Filterpapier, welches durch die Dämpfe sehr schnell entfärbt wird.

Patentansprüche:

1. Kontrollindikator für die Gassterilisation zur Prüfung des erfolgten Sterilisationsprozesses mit Perkarbonsäuredämpfen, vorzugsweise Peressigsäuredämpfen, bestehend aus z. B. Filterpapier, welches mit bestimmten Farbstofflösungen festgelegter Konzentration getränkt und anschließend getrocknet ist, gekennzeichnet dadurch, daß die Farbstofflösungen einen oder mehrere oxydativ schnell ausbleichbare Farbstoffe enthalten.
2. Kontrollindikator nach Anspruch 1, gekennzeichnet dadurch, daß die oxydativ schnell ausbleichbaren Farbstoffe vorzugsweise Kristallviolet, Viktoriablau, Chinablau, Baumwollblau, Gentianaviolett, Methylviolet, Lichtgrün, Malachitgrün, Diamantfuchs, Fuchs basisch, oder Fuchs sauer sind.
3. Kontrollindikator nach Anspruch 1 und 2, gekennzeichnet dadurch, daß die Farbstofflösung vorteilhafterweise eine 0,5%ige Lösung von Kristallviolet in Wasser ist.

Anwendungsgebiet der Erfindung

Die Erfindung betrifft einen Kontrollindikator für die Prüfung der erfolgten Behandlung bei der Gassterilisation von Gegenständen und Instrumenten, insbesondere von wärmeempfindlichen Instrumenten in einer geschlossenen Kammer, bzw. in einem Autoklav. Die Anwendung erfolgt insbesondere in Einrichtungen des Gesundheitswesens sowie in der pharmazeutischen Industrie.

Charakteristik des bekannten Standes der Technik

Zu den bereits bekannten und lange in Anwendung befindlichen Verfahren der Gassterilisation mit Ethylenoxid und Formaldehyd ist nun die Gassterilisation mit Perkarbonsäuredämpfen hinzugekommen. Bekannt ist die biologische Kontrolle der Gassterilisatoren mit speziell präparierten Sporen von *Bacillus subtilis* oder *Bacillus stearothermophilus*, die in festgelegten Zeitabständen, z. B. halbjährlich, durchgeführt werden müssen, wobei eine größere Anzahl von Sporenstrips über den ganzen Sterilisatorraum zu verteilen sind und zur Feststellung der Funktionsfähigkeit des Sterilisators mehrere Tage bebrütet werden müssen. Damit kann jedoch keine Aussage darüber getroffen werden, ob die zu sterilisierenden verpackten Gegenstände den Sterilisationsprozeß bereits durchlaufen haben. Kontrollindikatoren, auch als Behandlungsindikatoren bezeichnet, für die Gassterilisation mit Perkarbonsäuredämpfen sind nicht bekannt.

Ziel der Erfindung

Es ist das Ziel der Erfindung, für die tägliche Sterilisation mit Peressigsäuredämpfen in einer Kammer bzw. einem Autoklav einen Indikator zur Verfügung zu stellen, der die stattgefundene Behandlung anzeigt und damit Verwechslungen mit noch un behandeltem Sterilgut vermeidet.

Darlegung des Wesens der Erfindung

Aufgabe der Erfindung ist es, zur Kontrolle der stattgefundenen Behandlung des verpackten Sterilgutes mit Peressigsäuredämpfen einen Indikator bereitzustellen, der durch optisch leicht erkennbare Veränderung die stattgefundene Behandlung anzeigt, damit Verwechslungen mit noch un behandeltem Sterilgut vermeidet und somit eine schnelle Behandlungskontrolle gewährleistet. Da die Geschwindigkeit des Entfärbevorganges je nach der Oxydationsbeständigkeit des gewählten Farbstoffes verschieden ist, galt es einen Farbstoff zu finden, der kurzzeitig entfärbbar ist und sich somit für einen hochwertigen Kontrollindikator eignet.

Erfindungsgemäß wird die Aufgabe dadurch gelöst, daß die starke oxydierende und ausbleichende Wirkung der Peressigsäuredämpfe auf bestimmte dafür geeignete Farbstoffe genutzt wird.

Erfindungsgemäß wird eine 0,5%ige Kristallvioletlösung in Wasser benutzt. Weiterhin können z. B. folgende wäßrige Farbstofflösungen aus Viktoriablau, Chinablau, Baumwollblau, Gentianaviolett, Methylviolet, Lichtgrün, Malachitgrün, Diamantfuchs, Fuchs basisch, Fuchs sauer zur Anwendung gelangen.

Der Indikator wird auf der sterilhaltenden Verpackung befestigt und/oder in die Verpackung hineingelegt.

Ausführungsbeispiel

Das zur Herstellung des Indikators anzufärbende Filterpapier wird für etwa 5 min in die entsprechende Farblösung eingetaucht und anschließend z. B. durch Aufhängen an der Luft getrocknet.

Nach P. G. Simon, Hygiene + Medizin 12 (1987) 416, sollen Chemoindikatoren eine Mindestfläche von 1 cm^2 , höchstens jedoch $3,5 \text{ cm}^2$ haben. Sie werden auf der sterilhaltenden Verpackung befestigt und/oder in die Verpackung hineingelegt. Die hergestellten Kontrollindikatoren sind gut lagerbeständig, wenn sie nicht langzeitig dem direkten Sonnenlicht ausgesetzt werden.

Bei 45°C und einem Anfangsvakuum von $2,56 \text{ kPa}$ ($= 20 \text{ mm Hg}$) wird von den Peressigsäuredämpfen in einem gläsernen Exsikkator mit 0,5%iger Kristallvioletlösung getränktes Filterpapier in 5 bis 10 min völlig entfärbt.

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Patentee: Medical Academy Erfurt,
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Title: A Sterilization Indicator for the Gas-Sterilization

Keywords:

Sterilization indicator, autoclave, gas-sterilization, percarboxylic acid vapors, peracetic acid vapors, eosin, methylene blue, oxidative decolorization.

Abstract:

A sterilization indicator is described for the gas-sterilization of objects and instruments with percarboxylic acid vapors, preferably peracetic acid vapors, in a closed chamber or in an autoclave, respectively. The application occurs in particular in health-care facilities, as well as also in the pharmaceutical industry. The sterilization indicator for testing the sterilization process consists e.g. of a filter-paper strip impregnated with an eosin- or methylene blue solution, which will be gradually but completely decolorized due to the oxidative effect of the percarboxylic acid vapors. The time of the decolorization will be adjusted to be in agreement with the sterilization time by selecting a suitable dye and a suitable dye concentration.

PATENT CLAIMS

1. A sterilization indicator for the gas-sterilization for testing the sterilization with percarboxylic acid vapors, preferably peracetic acid vapors, consisting e.g. of a filter paper impregnated with certain dye solutions of a defined concentration and subsequently dried, wherein the dye solutions contain one or several oxidatively bleachable dyes.
2. A sterilization indicator according to claim 1, wherein the oxidatively bleachable dyes preferably consist of eosin B, eosin G, methylene blue DAB 7 *), methylene blue B extra, methylene green, amidoblack 10B **) or rhodamine.
3. A sterilization indicator according to claim 1 and 2, wherein the dye solutions advantageously consist of a 1% solution of eosin B, or a 2% solution of eosin G, or a 0.02% solution of methylene blue DAB 7 *), or a 0.01% solution of methylene blue B, extra, in water.

*) DAB 7 means "German Pharmacopeia, 7th. edition" -- HLS

**) Amidoblack or amido-schwarz is better known in the English literature as "Naphthol Blue Black" or also "Acid Black 1", C.I. 20470. -- HLS

Application Field of the Invention

The invention deals with a sterilization indicator for the testing of the gas-sterilization of objects, in particular heat-sensitive instruments, in a closed chamber, preferably an autoclave. The application occurs in particular in health-care facilities, as well as in the pharmaceutical industry.

Characteristics of the known State of the Art

In addition to the already known processes, which have been in practical use for a long time, such as the gas-sterilization process with ethylene oxide and formaldehyde, the gas-sterilization with percarboxylic acid vapors has been introduced. Furthermore, the biological control of the gas-sterilizers with specially prepared strips of *bacillus subtilis* or *bacillus stearothermophilus*, has been well known, whereby this control is to be performed in defined time intervals, e.g. semi-annually, by placing a larger number of these test-strips at the various locations within the sterilization chamber. For the daily application in a hospital practice, these types of bio-indicators are uneconomical, since an incubation time of several days is needed for evaluating the desired sterilization effects. Besides, the bio-indicators have only a limited life and have to be stored at 2 - 8°C.

A conclusion in regard to the sterility of packaged objects or instruments, respectively, can thereby not be drawn. Sterilization indicators for the gas-sterilization with percarboxylic acid vapors have not been known. Therefore, in particular if considering a centralized supply of sterilized objects and materials, the physician cannot be reliably assured, that the sterilization has been effectively performed in an economical manner.

Objectives of the Invention

The objectives to be achieved by the invention deal with the development of an indicator for the daily sterilization with peracetic acid vapors in a closed chamber or an autoclave, respectively, whereby the occurred sterilization process will be economically and optimally indicated or whereby the sterilization effect may be immediately evaluated after the performed sterilization process, respectively, and whereby the physician will be provided with this information with the greatest possible reliability without requiring costly procedures.

Presentation of the Essence of the Invention

The objectives of the invention deal with the development of an indicator for testing the sterilization of the sterile-packaged objects and materials with e.g. peracetic acid vapors, whereby the indicator will assure a fast sterilization control by optically readily recognizable changes in the appearance. Since the rate of the decolorization process is different depending on the stability of the particular dye against an oxidation, a dye had to be found, which is suited for a high-quality sterilization indicator. The objectives have been achieved according to the invention by utilizing the strong oxidizing and bleaching effects of the peracetic acid vapors on dyes suited for this purpose.

The sterilization is advantageously carried out at an initial vacuum of 2.66 KPa (= 20 mmHg) and at the preferred sterilization temperature of 45°C for a time of 1 hour. Dyes are employed, which will only be completely bleached within 1 hour under these conditions. According to the invention, 1% eosin B (2,7-dinitro-4,5-dibromofluorescein sodium) or 2% eosin G (2,3,5,7-tetrabromofluorescein sodium) or 0.02% methylene blue DAB 7, or 0.01% methylene blue B, extra, are dissolved in water. Furthermore, dye solutions of methylene green, amidoblack 10B or rhodamine may also be employed. The indicators will be attached on the packages to be sterilized and/or be placed in the packages.

Execution Examples

The filter paper to be used for the preparation of the indicator, will be immersed into the respective dye solution for about 5 minutes and subsequently after a brief drip-drying, will be dried e.g. by a suspension in air. According to *P.G. Simon, Hygiene and Medicine* 12, 416 (1987), chemical indicators are to have a minimal surface area of 1 cm², but not more than maximal 3.5 cm². These indicators are attached onto the packages to be sterilized and/or placed into the packages.

The employed dye concentration has an effect on the rate of the oxidative decolorization (bleaching) in the sense, that a stronger coloration due to a higher dye concentration, will require a longer bleaching time and vice versa. Weaker dye solutions will bleach much faster. However, the concentration effect is relatively small with the two eosin types, while very large with methylene blue.

Most suitably, the following dye concentrations are to be employed:

Eosin B (= eosin scarlet):	1%,
Eosin G:	2%,
Methylene blue, DAB 7:	only 0.02%,
Methylene blue B, extra:	only 0.01%.

The progressive decolorization of the red eosin sterilization indicators or of the blue colored methylene blue sterilization indicators, as well as of other chemo-indicators, could be continuously observed in a glass desiccator containing saturated vapors of peracetic acid. The colored filter paper strips were placed on the perforated porcelain plate and were examined at 45°C under a reduced pressure.

The prepared colored chemo-indicators exhibit a very good storability, if not directly exposed to sunlight for a longer period of time.

Some other relatively oxidation resistant dyes are also suited for the preparation of sterilization indicators, such as e.g. methylene green, amidoblack 10B or rhodamine.

In the following table, the results of a decolorization with peracetic acid vapors are summarized, as observed in a glass desiccator at 45°C and an initial vacuum of 2.66 KPa (= 20 mmHg).

Filter Paper impregnated with	Color	Decolorized after
1 % Eosin B	scarlet red	about 1 hour
2 % Eosin G	red	about 1 hour
0.01 % Methylene blue B extra	blue	about 1 hour
0.02 % Methylene blue DAB 7	blue	about 1 hour

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